Original Research Article

A comparative study of theta wave in quantitative EEG among ADHD children with or without methylphenidate treatment

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Received: 29-11-2021 / Revised: 24-12-2021 / Accepted: 01-01-2022

Abstract

Aims and Objective: To assess and compare QEEG findings (mean absolute power values of theta wave) between Patients on Methylphenidate and Drug naive ADHD patients. **Methodology:** A total no of 78 participants included in the study 26 in each group (Drug naïve ADHD children, ADHD children taking methylphenidate more than 3 months and healthy controls). Participated in the study after taking informed consent, scalp EEG was done and then fourier transformation was done by using BESS (brain electro scan software) of the Axxonet System (India).Statistical analysis was done using SPSS software. **Results:** In QEEG**,** mean absolute power value of theta wave found increased in frontal area electrodes in ADHD children comparing to ADHD participant who were on methylphenidate treatment more than 3 months, which was statistically significant. **Conclusion:** Use of Quantitative EEG can allow researchers to more precisely understand the brain origins and increase understanding of Pathophysiology.

Keywords: ADHD, frequency

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is the most common neurodevelopment disorder among children and adolescents with a prevalence approaching 11% and is characterized by symptoms of inattention and/or hyperactivity and impulsivity, which have negative effects on academic, social, and occupational functionality as well as executive functions or emotional regulation[1]. Three types of ADHD are identified in theDSM-5as:

- Predominantly Inattentive Type (ADHD-PI or ADHD-I)
- Predominantly Hyperactive or Hyperactive-Impulsive Type (ADHD-PH or ADHD-HI)
- Combined Type (ADHD-C)

Early diagnosis and intervention are important to prevent functional impairment of ADHD as well as choosing the optimal treatment options among alternatives such as stimulants, atomoxetine, clonidine, and guanfacine[2]. For example, severe ADHD and low IQ factors were associated with low response rate but their predictive ability is limited[3]. Based on family history, genotyping and neuro-imaging studies, there is clear evidence to support a biological basis for ADHD. Many hypotheses have been suggested to explain ADHD symptoms including theories of abnormal arousal and poor ability to modulate emotions. This theory was initially supported by the observation that stimulant medications increased sustained attention and improve focus.

Another biomarker that could be used to predict response is quantitative EEG (QEEG)[4]. QEEG - a field concerned with numerical analysis of EEG data and associated behavior correlates.

The interpretation is straightforward as electrical activity of the brain recorded with electrodes on the scalp are converted into common]. frequency bands, which are alpha, beta, delta, and theta[5Most children with ADHD display fairly consistent EEG differences in brain electrical activity when compared to normal children, particularly regarding frontal and central theta activity, which is associated with underarousal and indicative of decreased cortical activity (Chabot & Serfontein, 1996;Clarke, Barry, McCarthy, & Selikowitz, 1998, 2001a; El-Sayed, Larsson, Persson, & Rydelius, 2002;Lazzaro et al., 1998). In the largest EEG study of ADHD to date (with a sample of over 400 children),Chabot and Serfontein (1996) found that children with ADHD displayed increased theta power, slight elevations in frontal alpha power, and diffuse decreases in beta mean frequency. Increased theta power is the most consistent finding in this ADHD EEG literature, indicating that cortical hypoarousal is a common neuropathological mechanism in ADHD[6]. Nevertheless, there are also meta-analysis showing that theta/beta ratio may not be elevated in all children with ADHD. Various treatment options among alternatives such as stimulants like methylphenidate, dexmethylphenidate ,dextroamphetamine, amphetamine salts, non-stimulants like atomoxetine, alpha adrenergic agonists like clonidine, and guanfacine and bupropion preparations. Methylphenidate is a psychostimulant medication that blocks the transporters for both norepinephrine and dopamine (NET and DAT). Besides diagnosis, QEEG could also be used to predict treatment response. Several studies explored the use of QEEG in the prediction of response to medication in patients with depression, obsessive-compulsive disorder, and schizophrenia.There are also a number of studies exploring the role of QEEG as a biomarker for prediction of response to stimulants[7]. Previous studies suggest that QEEG features may be useful as biomarkers for predicting treatment response in ADHD. However, the results of the previous studies are contradicting and inconsistent.

Aims and Objectives

To assess and compare QEEG findings (mean absolute power values of theta wave) between Patients on Methylphenidate and Drug naive ADHD patients.

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Materials and method

A total no of 78 participants included in the study 26 in each group (Drug naïve ADHD children, ADHD children taking methylphenidate more than 3 months and healthy controls).

Study Design

A cross sectional hospital based Analytic type of Observational study carried out between April 2020 and August 2021 on patients of ADHD attending at psychiatric center, department of psychiatry, SMS medical college & hospital, Jaipur. Ethical Consideration was taken from research review board & ethical committee of the institution. Study included cases of ADHD [diagnosed as per DSM – V criteria] satisfying inclusion criteria and exclusion (via screening Performa).

Selection criteria

Inclusion Criteria

1. Children aged between 6 to 17 yrs
2. Level of intelligence (IQ >70)
3. Either sex
4. Patient diagnosed as ADHD according to DSM 5
5. Whose parents are willing to participate and ready to give written informed consent.

Exclusion criteria

1. Child having any psychiatric disorder
2. Child having autism spectrum disorder.
3. Seizure episode in the past.

Quantitative EEG

The EEG recordings were run for 5 minutes for each of the maneuvers with the subjects at rest, with eyes closed. Informed written consent was obtained from all the control and ADHD children's parents or the guardian who were enrolled in the present study. The subjects and patients so included in the study were asked to wash their hair the night before the EEG test run and not apply anything (hair cream, oils or spray) after the shampoo.

The EEG was recorded on the 20 leads- FP1,FP2,F3,F4,F7,F8,FZ,C3,C4,CZ,T3,T4,T5,T6,P3,P4,PZ,O1,O2,OZ.

Impedance was kept below 5 Ω and electrical activities, amplified with a band- pass filter of 0.5 - 30.0 Hz, were digitized at sampling rate 256 Hz. Recording of EEG was taken in a sound attenuated, dimly lit room. QEEG was done for all the participant using BESS (brain electro scan software) of the Axxonet System (India). Artifacts free epochs of 3 seconds each were chosen because after every of 2-3 seconds the changes both inclusive and exclusive in the amplitude were taking place more than 10% and their pectral content evaluated by means of Fast Fourier Transform analysis.

Statistical analysis

The data were coded and entered into Microsoft Excel spreadsheet. Quantitative variables were expressed as Mean ± SD. Analysis was done using SPSS version 17.0 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Significance of difference in mean in three groups was inferred by "ANOVA test". Statistical significance was assigned at p-value of less than 0.05.

Results

Socio demographic data

The age distribution was almost same among all three groups .Mean age respectively in Drug naïve ADHD children is 11.35 yrs , ADHD children taking methylphenidate more than 3 months is 9.35 yrs and healthy control is 12.88 yrs. Participants were mostly from urban background and education level was primary of most participants. Mostly participants were belonged to Hindu religion.

Frontal region

	Without MT		With MT		Control		Result (p value)
	Mean	SD	Mean	SD	Mean	SD	
FP1	299.20	1.43	165.24	7.54	120.84	9.92	p<0.001*
FP2	240.62	19.10	168.90	6.76	129.06	7.92	p<0.001*
F3	216.80	4.88	165.73	5.44	119.77	7.37	p<0.001*
F4	202.95	5.76	162.08	5.31	105.64	7.09	p<0.001*
F7	205.27	21.11	138.39	6.24	89.15	5.52	p<0.001*
F8	183.84	4.45	131.69	6.03	84.38	7.94	p<0.001*
FZ	129.40	5.13	129.63	4.43	111.16	8.86	p<0.001*

In our study, theta band in patients without MT at all levels FP1 to FZ was significantly higher as compared to patients with MT and control in frontal region. In methylphenidate treated group theta power values reduced and approximated to control group. This signifies that after methylphenidate treatment theta (slow) wave reduced in frontal region and approximated to control group.

Central region

	Without MT		With MT		Control		Result (p value)
	Mean	SD	Mean	SD	Mean	SD	
C3	135.74	5.23	135.47	3.65	137.90	6.29	0.183
C4	123.44	3.29	124.35	3.68	124.14	4.30	0.663
CZ	92.56	4.48	92.98	8.90	93.95	8.16	0.789

In central region theta power difference in all groups was found statistically insignificant

Temporal region

	Without MT		With MT		Control		Result (p value)
	Mean	SD	Mean	SD	Mean	SD	
T3	91.78	3.76	90.33	3.68	91.26	5.45	0.487
T4	109.91	7.50	106.11	4.07	108.53	9.25	0.168
T5	121.78	1.44	121.36	1.68	121.95	1.76	0.410
T6	139.97	2.51	139.73	2.11	140.25	3.97	0.817

In temporal region theta power difference in all groups was found statistically insignificant

Parietal region

	Without MT		With MT		Control		Result (p value)
	Mean	SD	Mean	SD	Mean	SD	
P3	122.63	3.40	122.71	3.21	122.44	3.26	0.953
P4	117.76	2.20	117.65	2.21	117.85	2.28	0.945
PZ	92.69	6.18	93.57	4.39	91.16	6.29	0.308

In parietal region theta power difference in all groups was found statistically insignificant

Occipital region

	Without MT		With MT		Control		Result (p value)
	Mean	SD	Mean	SD	Mean	SD	
O1	121.14	5.08	122.44	2.54	120.90	5.21	0.120
O2	94.93	1.73	95.80	1.76	97.92	6.94	0.105
OZ	107.79	4.36	108.05	3.10	107.78	5.82	0.971

In occipital region theta power difference in all groups was found statistically insignificant

Discussion

In present study we analyzed the power spectrum of theta frequency band (4 Hz to 7 Hz) during resting state EEG in eyes closed condition in children suffering from ADHD. This study investigated the Quantitative EEG differences in three different groups like drug naïve children suffering from ADHD, children taking Methylphenidate drug more than 3 months and healthy controls. These findings in QEEG in above mentioned three groups compared with each other. The results of the study showed that ADHD drug naïve group had more theta activities, especially in the frontal regions. Present study is supported by Ramazan Aldemir et al ,2018; Adam R. Clarke et al ,2002; Mann et al., 1992; Chabot and Serfontein, 1996; Clarke et al., 1998, 2001b,c;), who evaluated and found that Children with the Inattentive type of ADHD typically have increased theta activity in frontal region. The Power Spectral Density (PSD) of theta so observed in ADHD children in the present study was high and not commensurate with the documented PSD of theta in healthy control children.

In the present study, significant increase in absolute power of theta – form could be appreciated during the eye closed ($p < 0.001$) in children with ADHD when compared to that observed in normal healthy controls in the frontal EEG electrode pairs. The said frontal EEG electrode pairs reflect the underlying cognitive neural mechanisms sub serving attention and alertness.

The anomalous profiling of *theta and delta wave form* in ADHD children in real – time seems to be due to dysfunctional theta primarily in frontal lobe .

The data so observed in ADHD children support the premise that maturational delay implicates

dysfunctional attentional neural network that forms the mainstay of that children afflicted with blemish in attentional neuronal mechanisms and this is subsequently translated in the form of an enhanced absolute power of theta – form (statistically significant with predictive value of less than 0.005, $p < 0.005$) so observed in the frontal EEG electrode pairs .

In present study it has been found that the stimulant (Methylphenidate) used usually cause decrease in theta activity in frontal region and approximated to healthy control group. These findings are supported by Ramazan Aldemir et al, 2018; Adam R. Clarke et al, 2002; Stimulant medications produced changes in the EEG towards normalization, with reductions in absolute theta . Together, these results suggest that stimulants act to increase arousal in children who are cortically hypoaroused, resulting in a degree of normalization of their arousal levels. Present study contrary to Emel Sari Gokten et al, who analyzed the power spectrum of different frequency bands (delta, theta, and beta) during resting state EEG in eyes closed condition. They found that patients with higher slow oscillations, lower fast oscillations improved to a greater extent.

These findings indicate that patients with increased theta power at Fz, F4, C3, Cz, and T5 after methylphenidate (stimulant) medication showed more improvement in ADHD hyperactivity symptoms. This means, those with greater theta/beta and delta/beta powers showed more improvement in hyperactivity following medication .Identification of biomarkers predicting treatment response in ADHD is important with regard to an emerging concept. The personalized medicine approach prompts the use of genetic or neurobiological markers to tailor the healthcare decisions according to patient needs and peculiarities. In that sense QEEG markers could be used to individualize treatment and studies showed promising results for instance in depression[8,9], obsessive-compulsive disorder[10], anxiety disorders, and schizophrenia albeit the meta-analyses did not show any consistency[11,12]. With regard to ADHD, various studies emphasized that the increase in theta power and theta/beta ratio and the decrease in beta power can be a useful tool for the diagnosis of ADHD[13-16]. On the other hand, Arnset et al[17] established that theta/beta ratio cannot be a reliable assessment tool for the diagnosis of ADHD but it can be used as a tool, which may help monitor the prognosis in only one specific subgroup. As stated in the introduction, studies yielded mixed results on the role of fast and slow EEG oscillations for predicting the treatment response in ADHD.

To illustrate the inconsistencies in findings, one study[18] reported that decreased theta was associated with treatment response whereas another just reported the opposite. Yet another study showed no relationship between theta/beta waves and treatment response but found an association for alpha oscillations[19]. EEG studies of the effects of stimulant medications has produced inconsistent results. Swartwood et al. (1998) and Lubar et al. (1999) failed to find any significant changes in the EEG due to medication. These results indicate that although QEEG may be used as one of the several factors for predicting clinical response, based on the prediction accuracies, one would not advocate its use as a sole predictor of treatment response or that there may be intermediate mediating/ modulating factors which need to be studied in detail but they are not under purview of this study. The inconsistencies described above in EEG predictors of treatment response pose a challenge in front of personalized medicine attempts in psychiatry; however, the challenge may be overcome by using more sophisticated EEG analysis methods. Future studies should aim to find more accurate predictors that can be used solely to estimate response to stimulants. These predictors could involve use of multiple imaging methods at the same time[20].

Conclusion

In Quantitative Electroencephalography (QEEG) - mean absolute power at frontal area electrodes were found statistically significant for theta wave in between three groups. What has been researched in this study is not only whether QEEG is likely to support the diagnosis, but whether changes on QEEG by treatment may predict clinical response.

Acknowledgement
Nil

Conflict of Interest
Nil

Sources of support (including sponsorship)
Nil

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